

vector of claim 6. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 14, lines 12-15.

It will be understood that no new matter is included within the newly added claims.

### **III. Rejection of Claims 1-3 Under 35 U.S.C. § 101**

The Action first rejects claims 1-3 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present application describes a novel G-protein coupled receptor (GPCR). Of the pharmaceutical products currently being market by the entire industry, 60% of these drugs target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. 8:1257-1299). Given that more than half of the currently marketed drugs target proteins that are structurally (7TM proteins) and functionally (G-protein interaction) related to the presently described sequences, a preponderance of the evidence clearly weighs in favor of Applicants' assertion that the presently described sequences have a specific (the claimed GPCR proteins are encoded by a specific locus on the human genome), credible, and well-established utility.

The Action notes that the “disclosure fails to disclose the degree of homology . . . of the claimed molecules” (Action at page 3). Applicants would like to invite the Examiner’s attention to the fact that a sequence sharing over 90% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as “Homo sapiens similar to G protein-coupled receptor 56” (GenBank accession number XM\_169439). The alignment of these sequences is shown in **Exhibit C**. In fact, Applicants’ sequence appears to be a splice variant of XM\_169439, as the sequences are 100% identical at the protein level with the exception of the extra exon present in the XM\_169439 sequence. The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art would clearly believe that Applicants’ sequence is a G-protein coupled receptor.

Additionally, Applicants would like to invite the Examiner’s attention to the fact that a sequence

sharing 68% percent identity and 78% similarity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as “Mus musculus Pb99 gene sequence” (GenBank accession number AF249738). The alignment of these sequences is shown in **Exhibit D**. This protein is the murine homolog of the described human sequence, and has been characterized by the same third party scientists as a G-protein coupled receptor (2000, Mol. Cell. Biol. 20:4405-4410; see abstract, **Exhibit E**). As described above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and scientific publication, there can be no question that those skilled in the art would clearly believe that Applicants’ sequence is a G-protein coupled receptor.

The Action questions prediction of protein function based upon protein homology, citing Bork and Koonin (1998, Nature Genetics 18:313-318). However, Bork and Koonin themselves conclude “(i)n summary, the currently available methods for sequence analysis are sophisticated, and while further improvements will certainly ensue, they are already capable of extracting subtle but functionally relevant signals from protein sequences (Bork and Koonin, page 317). Thus, the Bork and Koonin article is hardly indicative of a high level of uncertainty in assigning function based on sequence, and thus does not support the alleged lack of utility.

The Action goes on to question asserted utility based upon such protein homology, citing Ji *et al.* (1998, J. Biol. Chem. 273:17299-17302; “Ji”) and Yan *et al.* (2000, Science 290:523-527; “Yan”) to support this argument. But an exact quote from Ji completely undermines this argument: “a substantial degree of amino acid homology is found between members of a particular subfamily, but comparisons between subfamilies show significantly less or no similarity” (Ji at 17299, first paragraph, emphasis added). This quote suggests that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that subfamily - the fact that there is little or no homology between subfamilies is completely irrelevant. Furthermore, regarding Yan, this paper cites only one example, two isoforms of the anhidrotic ectodermal dysplasia (EDA) gene, where a two amino acid change conforms one isoform (EDA-A1) into the second isoform (EDA-A2). However, while it is true that this amino acid change results in binding to different receptors, it is important to note

that the different receptors bound by the two isoforms are in fact related (Yan at page 523). Furthermore, the EDA-A2 receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based solely on sequence similarity (Yan at page 523). Thus, Yan does not suggest a high level of uncertainty in assigning function based on sequence, and thus also does not support the alleged lack of utility.

Rather, as set forth by the Federal Circuit, “(t)he threshold of utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit.” *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that “(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result.” *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); “*Cross*”) states “any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101”. *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that “anything under the sun that is made by man” is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), “*Brana*”), the Federal Circuit admonished the P.T.O. for confusing “the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption”. *Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

*Brana* at 1439, emphasis added. The choice of the phrase “utility or usefulness” in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using “utility” to refer to rejections under 35 U.S.C. § 101, and is using “usefulness” to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

*Brana* at 1442-1443, citations omitted. The Examiner states that “further research would be required” in certain aspects of the present invention (Action at page 4). However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit’s holding in *Brana*, which clearly states, as highlighted in the quote above, that “pharmaceutical inventions, necessarily includes the expectation of further research and development” (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988; “*Wands*”).

As just one example of utility of the present nucleotide sequences, Applicants point out that, as taught in the specification as originally filed, at least at page 33, lines 5-26, the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such “DNA chips” clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Evidence of the “real world” substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip

format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section IV, below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, as described above, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too

low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

The present invention has a number of substantial and credible utilities, not the least of which is in expanding the utility of data coming from the human genome project. The Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequences provide biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequences define how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of the Venter *et al.* article (Science, 2001, 291:1304 at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequences define biologically validated sequences that provide a unique and specific resource for mapping genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Furthermore, persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *supra*). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for compliance with 35 U.S.C. § 101. The PTO has issued numerous patents on polynucleotide sequences that have not been directly shown to be associated “with any disease or condition”, the condition apparently set forth by the Examiner as allegedly necessary to comply with 35 U.S.C. § 101. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,2812 (each of which claims short polynucleotide fragments), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring in the present Action. Additionally, the Office has recently issued U.S. Patent 6,043,052, which concerns an “orphan” G-Protein coupled receptor identified based only on homology to the orphan receptor GPR25, similar to the situation with Applicants’ currently claimed sequence. Importantly, this issued patent also contains no examples of the “real world” utilities seemingly required in the present case. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the presently claimed polynucleotide must also meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

#### **IV. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph**

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-3 have been shown to have “a specific, substantial, and credible utility”, as detailed in section III above, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

**V. Rejection of Claim 1 Under 35 U.S.C. § 112, First Paragraph**

The Action next rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 22 contiguous nucleotides of SEQ ID NO:43. Applicants respectfully traverse.

The Action admits that the specification is enabled for "SEQ ID NO:43 that encodes SEQ ID NO:44" (Action at page 6). The Action then states that "the disclosure has not provided sufficient guidance and information regarding the structural and functional requirements commensurate in scope" with the claim (Action at page 6, emphasis added).

Applicants point out that the above comment is irrelevant to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. Therefore, Applicants submit that the Examiner has failed to present reasoning sufficient to establish a *prima facie* case supporting the present § 112 rejection, and accordingly the rejection is improper because: 1) the Examiner's comments were not relevant to the established legal standard of enablement; 2) the Examiner's failure to attribute adequate weight and attention to the detailed level of teaching clearly provided in the specification; and 3) the reasoning for the enablement rejection provided by the Examiner failed to adequately consider the high level of technical knowledge that can be attributed to those skilled in the art in the field of the present invention.

**A. Enablement is Established by Enabling Any Practical Use**

In attempting to establish a *prima facie* case to support the § 112 rejection of the composition claims, the Action questions whether the claimed compositions are sufficiently enabled to allow those skilled in the art to practice aspects of the invention involving standard molecular biological techniques. The § 112 rejection, as applied against the nucleic acid compositions, is completely misplaced. It has long been established that composition claims are enabled by defining any practical use of the claimed compound. *In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, *supra*. "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns*



*Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). The Examiner has already conceded that “the nucleic acid molecule of SEQ ID NO:43 or encoding the amino acid sequence set forth in SEQ ID NO:44” is enabled (Action at page 6). Thus, the enablement issue should be resolved. Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, by the Examiner’s own admission, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed in Section III, above, in *In re Brana*, *supra*, the Federal Circuit admonished the P.T.O. for confusing “the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption”. *Brana* at 1442.

The Examiner cites *In re Wands* (*supra*) for the proposition that the present invention could not be practiced without “undue experimentation”. However, it is important to remember that, as discussed above in Section III, in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, *supra*. In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.’s rejection, the Federal Circuit found that *Wands*’ demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring ‘undue experimentation,’ even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or ‘hybridomas,’ since practitioners of art are prepared to screen negative hybridomas in

order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

*Wands* at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra*.

The Action cites Ngo *et al.* (1994, *The Protein Folding Problem and Tertiary Structure Prediction*, Merz *et al.* (ed.) Birkhauser, Boston, MA, pp. 433 and 492-495) for the proposition that “the relationship between sequence of a protein and its activity is not well understood” (Action at page 6). However, this argument is misplaced, because numerous uses of the claimed sequences do not require knowledge of any functional aspects of the amino acid sequences. Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section III, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

Even though the burden has been improperly shifted to Applicants, the following section is being provided to demonstrate that the specification is fully enabling in view of the detailed guidance and teaching provided in the specification within the context of the high level of technical knowledge present in the art regarding the use of nucleic acids such as those presently claimed.

## **B. The Specification Provides Adequate Guidance and Teaching**

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

*In re Marzocchi & Horton*, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra*. In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to be described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

### C. Claim 1 is Enabled

As detailed in the sections above, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

## VI. Rejection of Claim 1 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

Although [the applicant] does not have to describe exactly the subject matter claimed, ... the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

*Gosteli* at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph,

is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus “requires a precise definition, such as by structure, formula, chemical name or physical properties” sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; “*Fiers*”). *Fiers* goes on to hold that the “application satisfies the written description requirement since it sets forth the . . . nucleotide sequence” (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

In claims to genetic material ... a generic statement such as ‘vertebrate insulin cDNA’ or ‘mammalian insulin cDNA’, without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself*.

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing),

the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides comprising at least 22 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO:43 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claim 1 thus meets the written description requirement.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

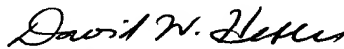
## **VII. Conclusion**

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

October 28, 2002

Date



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